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Impact of Cognitive Load on Family Decision Makers' Recall and Understanding of Donation Requests for the Genotype-Tissue Expression (GTEx) Project

Laura A. Siminoff, Maureen Wilson-Genderson, Maghboeba Mosavel, Laura Barker, Jennifer Trgina, Heather M. Traino, Howard M. Nathan, Richard D. Hasz, and Gary Walters

ABSTRACT

Genomic research projects that collect tissues from deceased organ and tissue donors must obtain the authorization of family decision makers under difficult circumstances that may affect the authorization process. Using a quasi-experimental design, the Ethical, Legal, and Social Issues (ELSI) substudy of the Genotype-Tissue Expression (GTEx) project compared the recall and understanding of the donation authorization process of two groups: family members who had authorized donation of tissues to the GTEx project (the comparison group) and family members who had authorized organ and tissue donations in years previous, who subsequently participated in two different mock-authorization processes that mimicked the GTEx authorization process (the intervention groups). Participants in the comparison and intervention groups were matched on key demographic characteristics.

We found that participants in the intervention groups who experienced a mock-authorization process demonstrated better

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recall of the tissue donation request than members of the comparison group. Our data indicate that the stress associated with the loss of a loved one limited the ability of family members to recall details about the GTEx project. However, we found a similar lack of knowledge in both the comparison and the intervention group participants, suggesting lack of knowledge may be due to the complexity and unfamiliarity of the information presented to them during the authorization process. We discuss these findings in the context of everyday clinical decision making in cognitively challenging conditions.

INTRODUCTION

The need for high-quality genomic data for medical research is growing.[1] A potentially plenteous source of the human material needed to support genomic research is through the generous donation of tissues from newly deceased patients by their family decision makers (FDM). The Genotype-Tissue Expression (GTEx) project is a leading-edge biobanking and genomic research project that provides high-quality gene expression data to study its impact on common diseases, that has successfully secured donations from the grieving FDMs of 961 deceased donors.[2] This mirrors the efforts of the National Institutes of Health's (NIH's) Precision Medicine Initiative (PMI) with living donors, as GTEx collects not only tissues but also links deceased donors' medical records and genomic information.

The Ethical, Legal and Social Issues (ELSI) study, which is a part of the GTEx project, has been pioneering best practices in requesting tissue samples and examining challenges to ensuring that these requests are conducted with sensitivity and in a manner that supports informed decisions about participation in GTEx.

The GTEx authorization process presented complex information about biobanking, genetic research, and confidentiality to FDMs after an initial conversation with them about donating the organs and or tissues of a deceased family member for transplantation.[3] The information was verbally delivered using a relatively brief script. Our initial pilot work with FDMs found that 29 percent of the families who were asked to donate to GTEx failed to remember that they were asked to donate for research, and 40 percent incorrectly believed that they would receive the results of the genetic tests.[4] Other studies of living donors have found similarly profound decrements in understanding and recall.[5]

Ensuring that FDMs understand the essential information needed to authorize the donation of organs and tissue—or of informed consent in the case of living donors—is especially salient in light of the growing need for increased participation in genomic research. For instance, NIH's groundbreaking PMI project will likely catapult the practice of precisely tailoring medical treatments to a patient's genomic profile through the participation of one million patients.[6] Additionally, the expansion of "personalized" medicine requires sustained investment in next-generation genomic and RNA (ribonucleic acid) sequencing projects that discover targeted disease treatments.[7]

Efforts to advance genomic profiling, with the goal of changing medical care, highlight the documented incongruence between the complexity of the information required to make an informed decision and the low levels of knowledge that have been observed in the general public. Asking individuals to participate in what may be an initiative that lays open their genomic information requires that we provide them with a higher level of education and information. This may entail using different and ongoing education and contact with the individuals that are well above our usual and common practice. Since the original President's Commission on Protection of Human Subjects published its *Reports of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research,* bioethicists have urged researchers to view obtaining subjects' informed consent not as a singular event in time, but as an ongoing process.[8] Especially in clinical research, most patients will participate in a study for months, and even sometimes years. Thus, obtaining ongoing consent could include checking in with patients periodically to discuss their trial participation experience and to affirm their willingness to continue their treatment within the context of the trial.

Despite these recommendations, informed consent continues to largely be practiced as a one-time-only event. While informed consent is not applicable in the context of requesting organ and tissue donation from a deceased individual, this study examined how the complexity of the information presented during the authorization process affects individuals' recall, and the implications for informed participation in modern genomic studies.

Factors Involved in Recall and Understanding

Cognitive Load Theory (CLT) offers potential insight into the problem of participants' recall and understanding.[9] CLT purports three dimensions of mental load: the complexity of the information (that is, *intrinsic load*), the complexity of the presentation of the information (that is, *extraneous load*), and the complexity of the schemas developed while

processing the information (that is, *germane load*).[10] The total burden imposed on decision making (that is, cognitive load) is comprised of the sum total of the mental load and the mental effort or attention given to the information that is presented. We posit that the combined effects of heightened emotions, exhaustion, extreme stress, and the volume of information that FDMs receive about organ and tissue donation, for both transplantation and research purposes, impedes their ability to process the information they receive, and their subsequent recall and understanding of the study's details.

In the case of the GTEx project, the highly technical genomic and medical research concepts presented to FDMs represented intrinsic load. Extraneous load was increased through the verbatim reading of an authorization document used to disclose the elements of informed consent regarding participation in the project. The intrinsic and extraneous load, in combination with the FDMs' already heightened emotions, impaired FDMs' ability to process information (germane load). This, in turn, resulted in compromised recall and comprehension of the information provided.

To better understand the processes involved, we employed a novel study design that manipulated the GTEx request environment to assess the degree to which the stress and grief associated with the death of a family member impacted cognition. Specifically, we compared FDMs' recall and understanding of a GTEx request for donation between two groups. The first—the comparison group—was comprised of FDMs who were asked to donate the patient's tissues to GTEx when they authorized the donation of the patient's solid organs. The GTEx requestors used a standard authorization script with this group.

The second group—the intervention group—was comprised of FDMs who experienced a simulated request for GTEx donation years after they experienced a request for solid organ donation. The intervention group was further split into two groups: the direct intervention group and the enhanced intervention group. For these two groups, the requestors used two different authorization processes (see figure 1); one of the processes replicated the request as received by the comparison groups and the other used an enhanced process.

The FDMs in the two intervention groups differed from the FDMs in the comparison group in that the FDMs in the intervention groups were not acutely grieving the loss of the patient, having experienced the donation request up to four years prior. On the other hand, the members of the intervention groups were highly comparable to the members of the comparison group, as they all had similar experiences of donation for transplantation. Members of the intervention group had the prior experience of making a donation decision that they could use as a framework for their experience with the hypothetical GTEx approach presented to them.

We were not primarily interested in the intervention groups' decisions to donate, as research indicates that decisions made in hypothetical scenarios may be affected by *hypothetical bias,* wherein participants overstate their valuations, their intention to act cooperatively, and their plans to act, as compared to their actual behavior in a real life context.[11] In this study, by removing the heightened emotional state of the members of the intervention groups, we were able to test whether grief and stress,

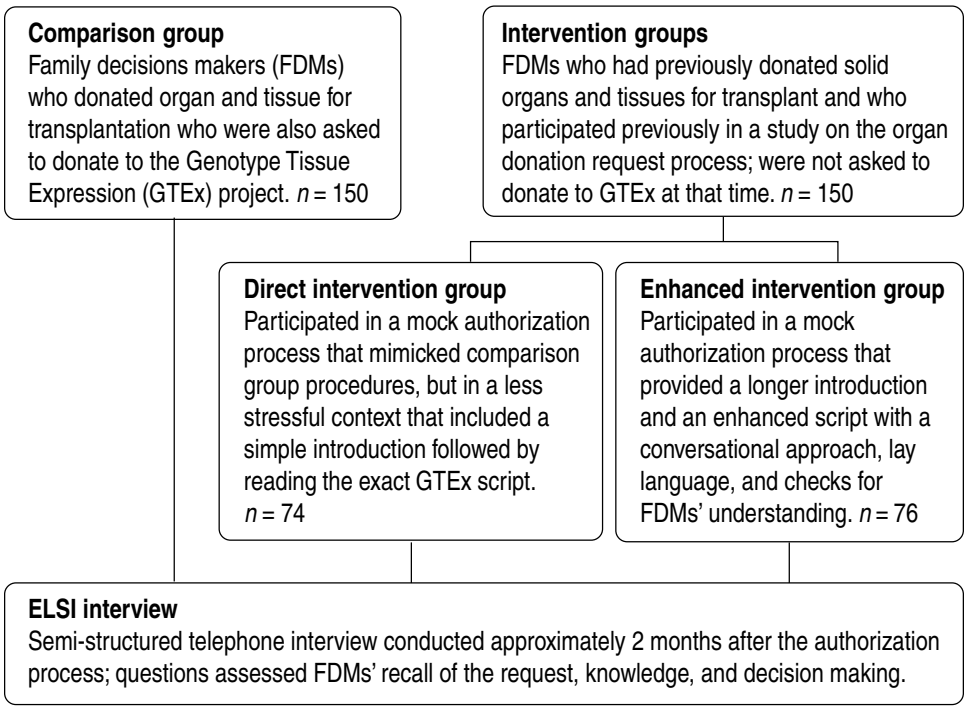

FIGURE 1.

versus the complexity of the information presented, were most highly associated with participants' recall and knowledge. We hypothesized that members of the comparison group, who received the standard GTEx request, would have worse recall and understanding than members of the intervention groups.

METHODS

GTEx Authorization Environment

The National Disease Research Interchange (NDRI) coordinated GTEx tissue collection activities and provided the ELSI team access to the contact information of all FDMs who were approached about the option of GTEx participation at five of the project's six geographically dispersed Organ Procurement Organizations (OPOs). Request staff were trained by NDRI and their OPO employers to approach FDMs about the option of donating to GTEx and to discuss aspects of tissue donation for research. A brochure explaining the purpose of the GTEx project and the extent and nature of participation were provided to participants who were approached in person. Requests made to FDMs for patients who were not eligible to donate solid organs for transplantation, but possibly to donate tissues, were made by telephone; these FDMs received a copy of the authorization form and, depending on its availability, the GTEx brochure. FDMs who authorized donation also agreed to the release of the patient's medical and social history records, various tissue samples, and, when medically suitable, the whole brain to GTEx. At the time of authorization, FDMs provided blanket authorization for unspecified future research and agreed to the sharing of aggregate data via the internet to NIH-registered researchers.[12]

Procedures

This study employed a nonrandomized quasi-experimental design with matched comparisons to determine whether FDMs' recall and understanding were affected either by the stressful *environment* in which GTEx requests were made or the *manner* in which the requests were made. OPOs made requests for GTEx to FDMs after they were asked to donate solid organs and tissue for transplantation. Organ donors and their families represent only a small subset of the population in the United States (it is estimated that only 1 to 2 percent of deaths in the U.S. are eligible to donate organs for transplantation).[13] To obtain a relevant intervention group, we randomly sampled from a cohort of families of organ donors who had participated in a previous study of the transplantation donation request process. These FDMs made organ donation decisions three to four years prior to the current investigation.[14] A matched comparison group was drawn from organ donor families who had been asked to donate tissues to GTEx subsequent to their decision to donate organs for transplantation. Thus, all participants had the same experience of being asked to donate a family member's organs. The comparison group had the additional experience of being asked to donate tissue for research to GTEx. The relevant difference between the comparison group and the intervention groups was the participants' environment during the GTEx request. Members of the intervention groups heard the GTEx request via a simulation delivered three to four years after they experienced a request for donation, and the comparison group received the GTEx request immediately after the request for transplantation at the time of the patient's death. This created two groups with different levels of stress and cognitive load during the request.

Two versions of the simulated request script were developed for the intervention groups by listening to audio recordings of actual telephoned GTEx requests from two participating OPOs. Because the first intervention group was intended to manipulate only the environment in which the request was heard, requests to members of this intervention group mimicked the OPOs' procedures for tissue requests by offering a short, general introduction to the project, followed by a verbatim reading of the authorization form (this is the direct intervention group). The requests made to the second intervention group mirrored the content of the presentation made to the first intervention group, but also manipulated the *delivery* of the request by including more lay language and incorporating several pauses and question prompts to check FDMs' understanding of the information provided to them (this is the enhanced intervention group). Once the presentations were developed, all five OPO partners reviewed and approved the simulated request scripts for fidelity to the OPOs' practices and the inclusion of all required elements for authorization. A single research assistant, trained to complete both types of requests, performed all of the simulated requests. All of the relevant institutional review boards approved this study, and verbal informed consent was obtained from all of the participants.

Study Samples. FDMs in the intervention groups were randomly selected and recruited from those agreeing to participate in a separate large national study examining the authorization process for organ donation (N = 1,503). In all, 373 of these FDMs were invited to participate in the intervention

groups, and 150 (40.2 percent) accepted the invitation and were randomly assigned to receive a presentation in either the direct intervention group (n = 74) or the enhanced intervention group (n = 76).

To generate a comparison group, each participant in the intervention groups (n = 150) was matched with an FDM enrolled in the ELSI substudy (n = 325) based on gender, race, age, income, education, religion, and marital status. Initially we aimed for perfect matching on gender and race and close matching on the remaining variables. This aim was achieved with a rate of 98 percent and 100 percent for gender and race variables, respectively. Male/female ratios were 40/110 and 43/107 for the comparison group and intervention groups, respectively.

Participants in both the comparison group and the intervention groups were recruited with invitational packets mailed to eligible FDMs (two months after a patient's death, in the case of the comparison group) using a protocol developed for analogous past research.[15]

Measurement

As part of their participation in the ELSI substudy, FDMs in the comparison group completed an hour-long, semistructured telephone interview two to three months after authorizing organ and tissue donation for transplantation and being approached for GTEx. The interview was developed and validated from our previous work with this population, and has been described in detail elsewhere.[16]

Upon enrollment in the current study, FDMs in the intervention groups were first prompted to recall their experience of being asked to donate their family member's organs and tissues. They were then asked to imagine a subsequent simulated request for GTEx immediately following that experience. After experiencing the simulated request, FDMs in both of the intervention groups were prompted for a decision about GTEx donation (agree/refuse). Two months after the simulated request, FDMs in the intervention groups were recontacted to complete a modified version of the interview used with the comparison group; the interview was shortened as appropriate to fit the unique experiences of these FDMs. Below we describe the variables relevant to the current investigation and their measurement.

Recall. Several questions assessed the participants' recall of the information provided about GTEx and biobanking. First, participants were prompted to recall two key terms (yes/no): (1) GTEx—the name of the study and (2) biobank—a term that was used frequently during the GTEx request. Participants were then provided a brief explanation of the project: "A biobank is a place where donated tissue samples are stored so that researchers can use them to study diseases. This biobank provides tissues to researchers to study how people's genes might play a role in their developing certain diseases. GTEx is the name of this biobank." The comparison group received additional information: "After you were asked to donate tissues for transplantation, the person who discussed transplantation with you also asked you to donate [patient's name]'s tissues to a biobank."

All of the participants were then asked whether they remembered the request to donate the patient's tissues to that research project (yes/no). A separate variable was created to indicate whether participants recalled the request before or after the explanation (0 = before/1 = after).

Knowledge/Comprehension. There were 17 questions asked that gauged respondents' understanding of the specific tissues that had been requested, the use of the tissues, participants' confidentiality, the potential linkage of the patient's tissues to medical records, the return of results, access to the samples, and the ability to withdraw the samples from the study (1 = true/0 = false). An index was created representing the number of questions a participant answered correctly. The questions are provided in the appendix at the end of this article.

Experimental Condition. The main independent variable was the condition under which the request was made to the participants. Three groups were generated. (1) The comparison group was comprised of FDMs who were asked to donate to GTEx immediately following a request to donate organs for transplantation. (2) The direct intervention group was comprised of FDMs who made a decision to donate organs for transplantation at the time of a loved one's death. Three to four years after the original donation request they were exposed to a simulated GTEx request using the same verbatim reading that members of the comparison group received. (3) The members of the enhanced intervention group were identical to that of the direct intervention group, except that the delivery of the GTEx request information used a conversational technique.

Statistical Analysis. Descriptive statistics were used to summarize participants' characteristics. Multivariate logistic regression was used to compare two groups at a time on three outcome variables simultaneously: (1) recall—before or after; (2) recall—GTEx; and (3) recall—biobank. Using a path-analytic specification of the model, all available data were used to estimate the model's parameters simultaneously, using the full information maximum like-

lihood method. Odds ratios (ORs) and their respective 95 percent confidence intervals (CIs) were used to present the results. Poisson regression was used to test group differences in the number of knowledge/comprehension items answered correctly.

RESULTS

Participants' characteristics are presented in table 1. Members of the comparison group and of the intervention groups were predominantly female, middle-aged, and White, with some college education. The matched samples had similar racial/ethnic make up, with 82 percent of each group identifying as White. To assess the success of matching, we reviewed seven matching variables and the patient's cause of death and found no significant differences between the groups (all p values > 0.10). Similarly, no significant differences were found between the two intervention groups (direct indirection versus enhanced intervention) on this set of variables (all p values > 0.10), indicating that the matching was successful.

The results of multivariate logistic regression are presented in table 2. Relative to the matched comparison group, members of the direct intervention

TABLE 1. FDMs' sociodemographics by group

	Intervention group					
Demographic characteristic	Comparison (n = 150)		Direct (n = 74)		Enhanced (n = 76)	
Income	$50 to $59K		$50 to $59K		$60 to $69K	
	Mean years	SD	Mean years	SD	Mean years	SD
Age	52.2	13.6	54.2	13.9	54.5	13.9
Education	14.4	2.3	14.7	2.3	14.4	2.1
	n	%	*n*	%	*n*	%
Sex—female	110	73.3	51	68.9	56	73.7
Race						
Black	17	11.3	5	6.8	10	13.2
White	123	82.0	63	85.1	60	78.9
Other	9	5.3	5	6.9	4	5.2
Marital Status						
Never married	19	12.7	6	8.1	9	11.8
Married/cohabit	48	32.0	32	43.2	24	31.6
Divorced/separated	9	6.0	7	9.5	7	9.2
Widowed	69	46.0	27	36.5	36	47.4
Religion						
Roman Catholic	34	22.7	20	27.0	20	26.3
Other	26	17.3	17	23.0	11	14.4
None	20	13.4	11	14.9	10	13.2
Relationship to patient						
Spouse	70	46.7	27	36.5	34	44.7
Parent	27	18.0	22	29.7	16	21.1
Sibling	22	14.7	6	8.1	12	15.8
Offspring	27	18.0	14	18.9	12	15.8
Other	1	0.7	4	5.4	2	2.6
Willing to donate own tissues—yes	140	93.3	65	87.8	72	94.7

Note: Percentages may not sum to 100 due to missing values. SD = standard deviation.

group were 38 percent more likely to recall the GTEx project before or after the explanation ($p < .001$), and 33 percent were more likely to recall the term biobank ($p < .01$). Similarly, members of the enhanced intervention group were nearly twice as likely to recall the term biobank ($p < .01$) than those in the comparison group. Members of the enhanced intervention group demonstrated considerably better recall of the term biobank than members of the comparison group (93 percent more likely; OR = 1.93). The direct intervention group also outperformed the matched members of the comparison group (33 percent more likely; OR = 1.33). While members of the enhanced intervention group who received an open reading of the script were more likely to recall the GTEx project before or after the explanation than were the matched members of the comparison group, the difference was not significant ($p > .10$). There were no statistically significant differences between the two intervention groups on their recall of the request or of the terms biobank or GTEx. Regarding the knowledge items, results from the Poisson regression indicated participants from neither intervention group exhibited significantly more knowledge than the respective matched members of the comparison group (all p values > .10).

DISCUSSION

Our data suggest that the limited recall and knowledge observed in FDMs who received the original, standard request for GTEx donation might have been due to the heightened emotions and/or physical fatigue that they experienced at the time of the request. The FDMs in both intervention groups had better recall of the GTEx project. However, participants' knowledge about the specifics of the research project—such as an understanding of the types of tissues requested, the use of the tissues, confidentiality, the potential linkage of the patient's tissues to medical records, the return of results, access to the samples, and the ability to withdraw samples from the study—were the same across the groups. This lack of understanding is not only disappointing, it is concerning, given the level of detail provided about deceased donors to hundreds and potentially thousands of researchers worldwide. Our results indicate that the reduction of the level of cognitive load and the stressful environment in the intervention group was helpful for recall, but the change from a standard to a more conversational approach to deliver information showed no appreciable improvement in participants' knowledge. Moreover, differences between the intervention groups were negligible. These results indicate that removal of acute emotional stress resulted in increased recall, but, despite this, the complexity and perhaps novel nature of the topic made it difficult for individuals who had little exposure to the topic to understand the information being delivered.

Studies of living biobanking participants indicate that donors often struggle to remember elements of informed consent, but generally have a good understanding of the basic purpose of the research project.[17] This study of surrogate decision making for deceased patients indicates that deceased donation presents increased challenges, compared to living donation. Future researchers who seek tissue from deceased organ and tissue donor FDMs should consider how they might lighten the intrinsic cog-

TABLE 2. Group comparisons

		Intervention group		
Outcome	Statistic	Direct intervention group = 0 versus enhanced intervention intervention group = 1	Comparison group = 0 versus direct invervention group = 1	Comparison group = 0 versus enhanced intervention group = 1
Recall GTEx—before or after	%	65.8 versus 68.9	**39.5 versus 65.8**	62.2 versus 68.9
	OR (95% CI)	1.09 (.71 to 1.67)	**1.38 (1.15 to 1.65)**	1.20 (.79 to 1.84)
Recall—term GTEx	%	30.3 versus 20.3	18.7 versus 30.3	33.8 versus 20.3
	OR (95% CI)	.80 (.51 to 1.24)	1.20 (.97 to 1.49)	.73 (.47 to 1.13)
Recall—term biobank	%	48.7 versus 59.5	**26.3 versus 48.7**	**33.8 versus 59.5**
	OR (95% CI)	1.31 (.87 to 1.38)	**1.33 (1.11 to 1.61)**	**1.93 (1.27 to 2.94)**

Note: Significant group differences are given in **boldface.** OR = odds ratio. CI = confidence interval.

nitive load (that is, the complexity of the information) and the extraneous cognitive load (that is, the presentation of the information) carried by FDMs who are approached for authorization.

One way to reduce the intrinsic load placed on FDMs when they review an authorization form is to simplify the text by shortening the request script, reducing the level of reading comprehension, and improving the layout of information contained in all of the documents used.[18] Most FDMs received information in oral form; written or modern infographic approaches might improve their recall and knowledge. Experts agree that the most important information necessary to make decisions about donation for genomic research projects should be presented first, potentially as bulleted lists.[19] Research indicates that spending more time discussing consent increases understanding.[20] The more-conversational reading of the simulated request script used in the enhanced intervention group was designed to include question prompts and probes to help requesters assess FDMs' understanding of the information they received. This version of the script also allowed for pauses and reduced the rate at which information was presented.

Given the findings of this study, these conversational techniques showed some promise to improve recall, but more techniques may be needed to help grief-stricken FDMs sufficiently grasp information about genomic and biobanking research projects. Continuous communication with willing, participating FDMs may be the best way to fully inform grief-stricken FDMs about the details and implications of their decisions. We recommend leveraging the use of OPO partners, who already routinely communicate with donor families, to disseminate this information to FDMs. The GTEx project is currently exploring options to send messages of thanks and updates from researchers to donor families via partnering OPOs.

An intervention with living biobanking participants indicates that increasing interactivity during the request and informed consent processes by embedding multiple-choice questions for participants in the conversation and providing immediate feedback to staff improved participants' understanding in face-to-face and multimedia formats.[21] Further, we suggest training tissue requesters (TRs) to hold long-form, "off-script" conversations with FDMs about critical authorization elements prior to a verbatim reading of the authorization form. A national resource to train TRs to communicate effectively with grieving families about genomic research has been developed out of the findings from the GTEx project's ELSI study, and a pilot of such an intervention is currently being tested.

It is important to note that FDMs in the comparison group who were matched to FDMs in the direct intervention group exhibited the lowest levels of recall of GTEx. Given the success of the matching process and the lack of difference between the members of the direct intervention group and their matched members of the comparison group and the other groups, it is not clear why recall was lower for that subsample. More research is needed to understand the specific aspects of the authorization process that are best understood by participants and the concepts that FDMs find difficult to grasp.

Nonetheless, these findings have important implications for clinical practice. First, our findings could be applied to any surrogate decision-making situation wherein a surrogate is under an immense amount of stress and trauma, including decisions made in emergency rooms and intensive-care units about the treatment of patients and their participation in research.[22] These results are also directly applicable to the context of cadaveric donation. Clinicians regularly approach and request cadaveric donations[23] and anatomical dissection for medical education and research from grieving families.[24] These donations remain critically important to medical education and doctors' knowledge of anatomy;[25] however, there is a shortage of cadavers. Research indicates there is little public understanding of this type of donation, and programs often rely on unclaimed bodies.[26] Similar to requesting research donations from FDMs, there is no gold standard for making other cadaveric donation requests, and very few ethical guidelines.[27] Our findings and the model of authorization provided by the GTEx project provide some framework for approaching decedents' family members for cadaveric donation.[28] First, clinicians may find it helpful to approach discussions regarding requests for cadaveric and other posthumous donations mindful that the cognitive load borne by patients' next of kin may impede their understanding of this type of donation, especially of complicated details. That FDMs have full understanding of these requests is especially relevant, considering that cadaveric donation may entail potentially disturbing uses of a decedent's body, such as crash testing or body decay, and finding this out after donation may cause physiological harm to family members.[29] Second, the need to fully communicate the risks and benefits of genomic research with decedents, an area of little oversight or ethical guidance[30] to their living relatives, is also pertinent to cadaveric donation.

This study is the first to experimentally test the impact of the authorization environment and the delivery of information on biobanking participants' recall and understanding, but it does have limitations. We asked participants to access their long-term memories for recall of terms and concepts in the GTEx authorization process, which is an imperfect measure of FDMs' understanding at the time of authorization; greater differences between the comparison group and the intervention groups may have been observed if we had assessed recall immediately following the donation authorization process. Additionally, our study design makes it impossible to distinguish between recall bias, in which members of the subgroups present nonrandom differences, and simple recall error or memory lapses.[31] However, the study design, which incorporated a conversational, interactive intervention group, demonstrated a potential to reduce the likelihood of recall error, and underscores the importance of the emotional environment to FDMs' ability to recall. It also highlights how complex and unfamiliar this area is to the general public. This lack of familiarity diminishes the ability of individuals to understand information presented about biobanking. Finally, we did not measure FDMs' cognitive load during the donation authorization process, nor did we measure their familiarity with genomic research, GTEx, or biobanking prior to the donation authorization process. However, studies of laypersons' understanding of genomic research indicate major gaps in knowledge about these concepts.[32]

CONCLUSION

As we move forward into an era of large-scale, population-based genomic research that collects detailed, personal data consisting of complete genetic information, medical records, and psychosocial profiles, we need to revisit our standards that assure that participants in these studies understand what they are agreeing to. These issues loom large for studies such as GTEx, neurological studies of brain injuries, and PMI. Consent or authorization to these studies should move into the 21st century, and take advantage of technology that embraces notions of collaboration, engagement, and education of the public and FDMs as the research moves forward.

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NOTES

1. E.D. Green and M.S. Guyer, National Human Genome Research Institute, "Charting a Course for Genomic Medicine from Base Pairs to Bedside," *Nature* 470 (10 February 2011): 204-13.

2. GTEx Consortium, "The Genotype-Tissue Expression (GTEx) Project," *Nature Genetics* 45, no. 6 (June 2013): 580-5; GTEx Consortium, "Human Genomics: The Genotype-Tissue Expression (GTEx) Pilot Analysis: Multitissue Gene Regulation in Humans," *Science* 348, no. 6235 (May 2015): 648-60.

3 L.J. Carithers and H.M. Moore, "The Genotype-Tissue Expression (GTEx) Project," *Biopreservation and Biobanking* 13, no. 5 (October 2015): 307-8; L.J. Carithers et al., "A Novel Approach to High-Quality Postmortem Tissue Procurement: The GTEx Project," *Biopreservation and Biobanking* 13, no. 5 (October 2015): 311-9; L.A. Siminoff et al., "Family Decision Maker Perspectives on the Return of Genetic Results in Biobanking Research," *Genetics in Medicine* 18, no. 1 (January 2016): 82-8; L.A. Siminoff et al., "Confidentiality in Biobanking Research: A Comparison of Donor and Nondonor Families' Understanding of Risks," *Genetic Testing and Molecular Biomarkers* 21, no. 3 (March 2017): 171-7.

4 L.A. Siminoff, "Communicating Effectively About Donation: An Educational Intervention to Increase Consent to Donation," *Progress in Transplantation* 19, no. 1 (March 2009): 35-43.

5. M.L. Boccia, F.A. Campbell, B.D. Goldman, and M. Skinner, "Differential Recall of Consent Information and Parental Decisions About Enrolling Children in Research Studies," *Journal of General Psychology* 136, no. 1 (January 2009): 91-108; J. Mancini, "Consent for Biobanking: Assessing the Understanding and Views of Cancer Patients," *Journal of the National Cancer Institute* 103, no. 2 (19 January 2011): 154-7; A.K. Shelton et al., "Surrogate Consent for Genomics Research in Intensive Care," *American Journal of Critical Care* 18, no. 5 (September 2009): 418-26.

6. F.S. Collins and H. Varmus, "A New Initiative on Precision Medicine," *New England Journal of Medicine,* 372, no. 9 (26 February 2015): 793-5.

7. E.E. Schadt and L.M. Bjorkegren, "New: Network-Enabled Wisdom in Biology, Medicine, and Health Care," *Science Translational Medicine* 4, no. 115 (4 January 2012): 1-8.

8. President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, "Splicing Life: The Social and Ethical Issues of Genetic Engineering with Human Beings," 1982, *http://hdl.handle.net/10822/559376*; C. Grady et al., "Broad Con-

sent for Research with Biological Samples: Workshop Conclusions," *American Journal of Bioethics* 15, no. 9 (2015): 34-42; J. Kaye et al., "Dynamic consent: A patient interface for twenty-first century research networks," *European Journal of Human Genetics* 23 (2015): 141-6; H. Williams et al., "Dynamic Consent: A Possible Solution to Improve Patient Confidence and Trust in How Electronic Patient Records Are Used in Medical Research," *JMIR Medical Informatics* 3, no. 1 (2015): e3.

9. J. Sweller, "Cognitive Load during Problem Solving: Effects on Learning," *Cognitive Science* 2, no. 12 (April-June 1988): 257-85.

10. J.J. van Merrienboer and J. Sweller, "Cognitive Load Theory in Health Professional Education: Design Principles and Strategies," *Medical Education* 44, no. 1 (January 2010): 85-93.

11. I. Vlaev, "How Different Are Real and Hypothetical Decisions? Overestimation, Contrast and Assimilation in Social Interaction," *Journal of Economic Psychology* 33, no. 5 (2012): 963-72.

12. J.C. Keen and H.M. Moore, "The Genotype-Tissue Expression (GTEx) Project: Linking Clinical Data with Molecular Analysis to Advance Personalized Medicine," *Journal of Personalized Medicine* 5, no. 1 (5 February 2015): 22-9.

13. U.S. Government Information on Organ and Tissue Donation and Transplantation, "Organ Donation Statistics," *https://www.organdonor.gov/statistics-stories/statistics.html.*

14. Siminoff et al., "Communicating Effectively About Donation," see note 4 above; Siminoff et al., "Family Decision Maker Perspectives," see note 3 above.

15 L.A. Siminoff, N. Gordon, J. Hewlett, and R.M. Arnold, "Factors Influencing Families' Consent for Donation of Solid Organs for Transplantation," *Journal of the American Medical Association* 286, no. 1 (4 July 2001): 71-7; L.A. Siminoff, H.M. Traino, and N. Gordon, "Determinants of Family Consent to Tissue Donation," *Journal of Trauma and Acute Care Surgery* 69, no. 4 (October 2010): 956-63.

16. Siminoff et al., "Family Decision Maker Perspectives," see note 3 above.

17. C.A. McCarty, A. Nair, D.M. Austin, and P.F. Giampietro, "Informed Consent and Subject Motivation to Participate in a Large, Population-Based Genomics Study: The Marshfield Clinic Personalized Medicine Research Project," *Journal of Community Genetics* 10, no. 1 (2007): 2-9; K.E. Ormond et al., "Assessing the Understanding of Biobank Participants," *American Journal of Medical Genetics* 149A, no. 2 (February 2009): 188-98; A.K. Rahm, M. Wrenn, N.M. Carroll, and H.S. Feigelson, "Biobanking for Research: A Survey of Patient Population Attitudes and Understanding," *Journal of Community Genetics* 4, no. 4 (October 2013): 445-50.

18. A. Nishimura et al., "Improving Understanding in the Research Informed Consent Process: A Systematic Review of 54 Interventions Tested in Randomized Control Trials," *BMC Medical Ethics* 14, no. 28 (23 July 2013).

19. L.M. Beskow et al., "Informed Consent for Biobanking: Consensus-Based Guidelines for Adequate Comprehension," *Journal of Medical Genetics* 17, no 3 (March 2015): 226-33; L. Dorflinger, S.M. Auerbach, and L.A. Siminoff, "Predictors of Consent in Tissue Donation: Interpersonal Aspects and Information Provision During Requests by Phone," *Patient Education and Counseling* 91, no. 2 (May 2013): 161-6; Siminoff et al., "Family Decision Maker Perspectives," see note 3 above.

20. J. Flory and E. Emanuel, "Interventions to Improve Research Participants' Understanding in Informed Consent for Research: A Systematic Review," *Journal of the American Medical Association* 292, no. 13 (2004): 1593-601.

21 A. K Shelton, "A Computer-Based Education Intervention to Enhance Surrogates' Informed Consent for Genomics Research," *American Journal of Critical Care* 24, no. 2 (March 2015): 148-55; Siminoff et al., "Family Decision Maker Perspectives," see note 3 above.

22. Shelton et al., "A Computer-Based Education Intervention," see note 21 above.

23. M.C. Morris, S. Tanya, and G.E. Hardart, "Enrolling Brain-Dead Humans in Medical Research: Stakeholder Opinions," *AJOB Empirical Bioethics* 5, no. 4 (2014): 22-9.

24. S.K. Ghosh, "Cadaveric dissection as an educational tool for anatomical sciences in the 21st century," *Anatomical Sciences Education* 10, no. 3 (June 2017):286-99.

25. Ibid.

26. A. Garment, S. Lederer, N. Rogers, and L. Boult, "Let the dead teach the living: The rise of body bequeathal in 20th-century America," *Academic Medicine* 82, no. 10 (October 2007): 1000-5.

27. T.H. Champney, "A proposal for a policy on the ethical care and use of cadavers and their tissues," *Anatomical Sciences Education* 4, no. 1 (2011): 49-52; A. Winkelmann, "Consent and consensus—Ethical perspectives on obtaining bodies for anatomical dissection," *Clinical Anatomy* 29, no. 1 (2016): 70-7.

28. R.L. Walker, E.T. Juengst, W. Whipple, and A.M. Davis, "Genomic research with the newly dead: A crossroads for ethics and policy," *Journal of Law, Medicine & Ethics* 42, no. 2 (2014): 220-31.

29. Ibid.

30. Ibid.

31. S. Coughlin, "Recall Bias in Epidemiologic Studies," *Journal of Clinical Epidemiology* 43, no. 1 (1990): 87-91.

32. S.B. Haga et al., "Public Knowledge of and Attitudes toward Genetics and Genetic Testing," *Genetic and Testing and Molecular Biomarkers* 17, no. 4 (April 2013): 327-35; A.D. Lanie et al., "Exploring the Public Understanding of Basic Genetic Concepts," *Journal of Genetic Counseling* 13, no. 4 (August 2004); 305-20.

APPENDIX

Knowledge Questions

By signing the consent form, I would have been agreeing to donate [patient's name]'s tissues to a biobank.

By signing the consent form, I would have been agreeing to include [patient's name]'s medical records in the biobank.

By signing the consent form, the researchers who would use the donated tissue would know [patient's name]'s exact identity.*

If I signed the consent form and the donated tissue were used for a research project, I would have been told what they learned about [patient's name]'s health.*

By signing the consent form there would have been a slight risk that [patient's name]'s identity could be found out.

By signing the consent form and donating [patient's name]'s tissues, there would have been a slight risk that the identity of my family could be found out.

When a person agrees to participate in the GTEx biobank it means that he or she would have consented to use of his or her tissues for:
- Medical research
- Genetic research
- Any studies, now or in the future
- Just one study*
- Indefinite storage of donated tissue
- Inclusion in a government biobank
- Research outside of the U.S.
- Research with for-profit companies

If someone were to donate tissues to the GTEx biobank, he or she would have the ability to:
- Remove the tissues from the storage facility whenever he or she wants to.
- Ask that information from the donated tissues be deleted from a project in which it is actively being used.*
- Ask that the donated tissues not be used in any future research studies.

Note: * indicates the correct answer is "false."